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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of N. Cashman and M. Lehto

Examiner: Wang, Chang Yu

Application No.: 10/568,729

Art Unit: 1649

Filed: July 13, 2006

Confirmation No. 7149

Title: Epitope Protection Assay And Method For Detecting Protein Conformations

(Attorney Docket No. P 31,382 USA)

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*Katie Carlson*  
Katie M. Carlson

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Mail Stop: Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**REPLY TO RESTRICTION REQUIREMENT DATED JULY 11, 2008**

Dear Sir:

In response to the Examiner's Requirement for Restriction, as set forth in the Action dated August 24, 2007, Applicants elect with traverse to prosecute the claims of Group I, claims 1-16 readable thereon, which are directed to a technical feature of a method for detecting whether a candidate polypeptide is in a wild-type or non-wild-type confirmation. Applicants further elect the following species:

- i. prions as the target species, claim 2 readable thereon;
- ii. BSE as the target indication, claim 22 readable thereon;
- iii. peroxyinitrite as the blocking agent, claim 9 readable thereon; and
- iv. antibody against prions as the probing agent, claims 16, 17, and 19 readable thereon.

The species elections are also made with traverse.

Applicants confirm their right to file divisional applications which include the non-elected claims.

### **Traversal**

The Examiner asserts that the inventions of Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. The Examiner further states that the first claimed invention has no special technical feature that defines a contribution over Kim et al. (Free Rad. Biol. Med. 2002. 32:544-550). Thus, according to the Examiner, the first claimed invention cannot share a special technical feature with the other claimed inventions.

“With respect to a group of inventions claimed in an international application, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. The expression ‘special technical features’ is defined in PCT Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art.” M.P.E.P. § 1850.

Contrary to the Examiner’s assertions, the claim groups do share a technical feature which makes a contribution over the prior art.

According to the Examiner, Kim et al. discloses a method for detecting whether alpha-synuclein is in wild type or non-wild type conformation in the presence of copper and H<sub>2</sub>O<sub>2</sub>, “which meets the limitations of claim 1”. Kim et al. studied the effect of hydroxyl ions on aggregation of synuclein. Kim et al. treated monomeric synuclein either directly with hydroxyl ions or with a hydroxyl ion generator, in the form of Cu/Zn SOD + hydrogen peroxide. The hydroxyl ions had the effect of aggregating synuclein. The authors speculate that the hydroxyl

ions caused carbonylation of certain synuclein residues, perhaps causing the aggregation. In any event, the authors determine the “conformation” of synuclein by immunoblotting, and detect aggregation simply by a size shift (see Fig 1).

The Applicant respectfully submits that the limitations of claim 1 are not met by Kim et al. Claim 1 requires the steps of:

- (1) contacting the polypeptide with a blocking agent that selectively blocks accessible epitope;
- (2) removing blocking agent;
- (3) modifying the polypeptide to convert inaccessible target epitope to accessible target epitope; and
- (4) probing with a detection agent that binds selectively to the target epitope that was first protected and then rendered accessible.

There is no evidence or suggestion that Kim et al. convert inaccessible or blocked target epitopes to accessible target epitopes, and further no detection agent is provided that binds selectively to the target epitope, where the target epitope is first blocked then rendered accessible.

For example, contacting copper and/or H<sub>2</sub>O<sub>2</sub> with wildtype and aggregated synuclein will result in aggregation of wildtype synuclein and not blocking of accessible epitopes. Wildtype and aggregated synuclein will not be distinguished. Alternatively, contacting wildtype and aggregated synuclein with DNPH, which is used to derivatize carbonyl groups, does not “block” accessible epitopes but rather makes carbonyl groups visible to  $\alpha$ -DNP sera. Further there is no conversion of the inaccessible target using DNPH. In each case, the probing antibody still binds to both monomeric and aggregated synuclein. Accordingly, the method of Kim et al. is NOT useful to achieve the selective binding results required by the steps recited in claim 1. Accordingly, Kim et al. does not disclose the shared technical feature of the claim groups which makes a contribution over the prior art. Thus, applicants submit respectfully that the restriction requirement should be withdrawn.

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The Commissioner is authorized hereby to charge any fees or credit any overpayment associated with this Reply to Deposit Account Number 19-5425.

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An early and favorable Action is requested respectfully.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'M. S. Segal', written over a horizontal line.

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